"What is the best way to identify patients who have early keratoconus and are likely to progress?"

“Currently sensitive diagnostic criteria”

- Topometric asymmetry indices IHD and ISV
- Pachymetric asymmetry; Scheimpflug < OCT
- Epithelial profiles

“Currently sensitive CLINICAL criteria”

1-age

2-Vision and mode of correction

3-Cornea Thickness

?4(“soft” criterion: location of cone)

Prof. A. John Kanellopoulos, MD
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Key Kanellopoulos ectasia questions?

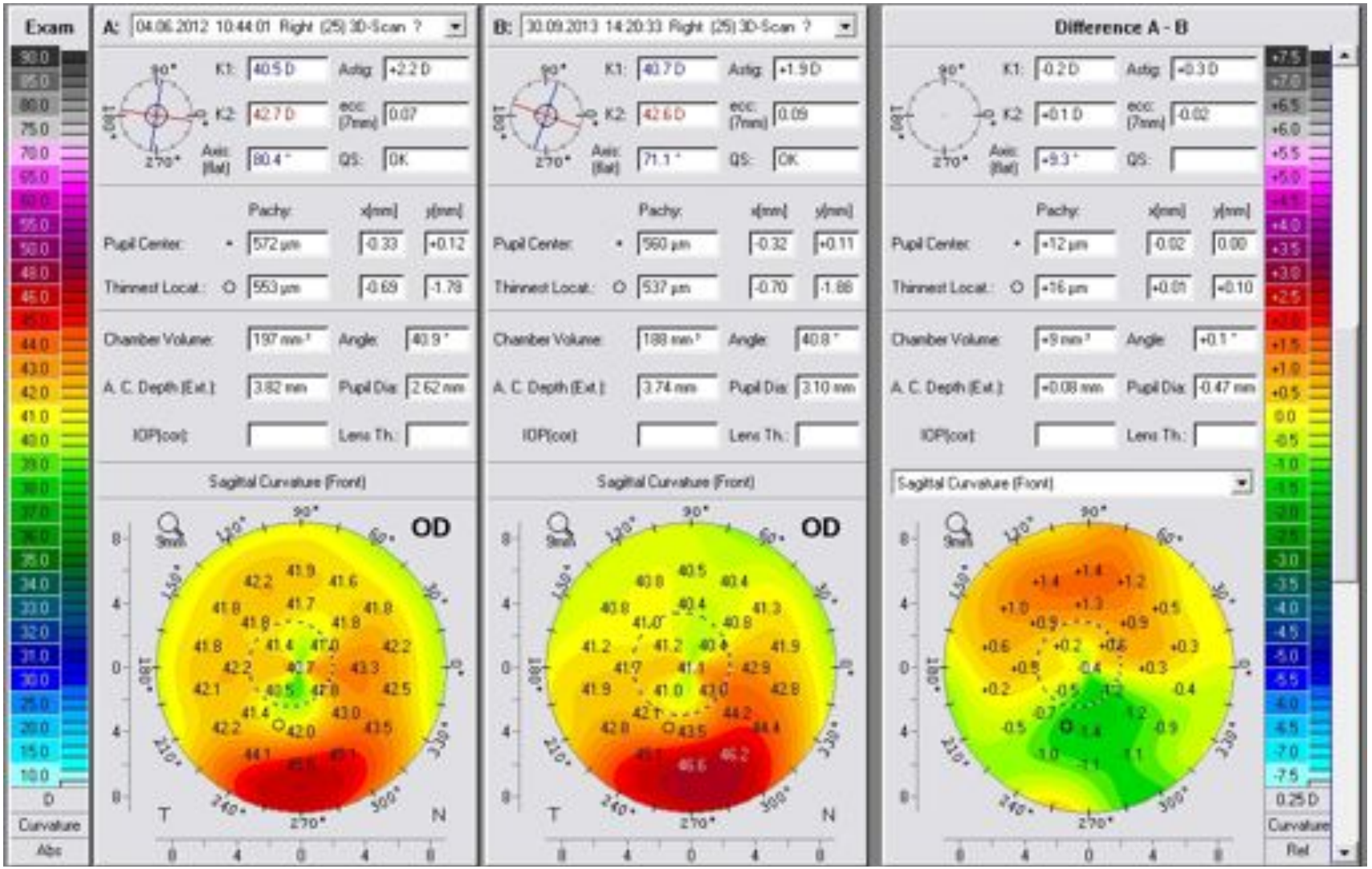
Does the thickness change first or does curvature change first?

Does anterior curvature change first or posterior?

Are corneas with “weaker” biomechanics in risk for ectasia? - or is there a “break” point in biomechanics different for EACH cornea in destabilizing it?

Routine measurements in my Clinical practice

- Topometric asymmetry indices IHD, ISV
- Pachymetric norms and asymmetry changes
- Epithelial remodeling
- Biomechanical measurements?
- View all topos in correlation with Biomicroscopy!
- Family topos important!!!


Exam
A: 04.06.2012 10:44:01 Right (25) 3D-Scan ?
B: 30.09.2013 14:20:33 Right (25) 3D-Scan ?
Difference A - B
K1: 40.5 D
K2: 42.7 D
Astig: +2.2 D
Axis (flat): 80.4°
ecc (7mm): 0.07
QS: OK
K1: 40.7 D
K2: 42.6 D
Astig: +1.9 D
Axis (flat): 71.1°
ecc (7mm): 0.09
QS: OK
K1: -0.2 D
K2: -0.1 D
Astig: -0.3 D
Axis (flat): +9.3°
ecc (7mm): -0.02
QS:
Pachy
x[mm]
y[mm]
Pupil Center: 572 µm -0.33 +0.12
Thinnest Locat.: 553 µm -0.69 -1.78
Pupil Center: 560 µm -0.32 +0.11
Thinnest Locat.: 537 µm -0.70 -1.88
Pupil Center: +12 µm 0.02 0.00
Thinnest Locat.: +16 µm +0.01 +0.10
Chamber Volume: 197 mm³ Angle: 40.9°
A. C. Depth (Ext.): 3.82 mm Pupil Dia: 2.62 mm
IOP[cor]: Lens Th.:
Chamber Volume: 188 mm³ Angle: 40.8°
A. C. Depth (Ext.): 3.74 mm Pupil Dia: 3.10 mm
IOP[cor]: Lens Th.:
Chamber Volume: +9 mm³ Angle: +0.1°
A. C. Depth (Ext.): +0.08 mm Pupil Dia: -0.47 mm
IOP[cor]: Lens Th.:
Sagittal Curvature (Front)
Sagittal Curvature (Front)
Sagittal Curvature (Front)
OD
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Curvature
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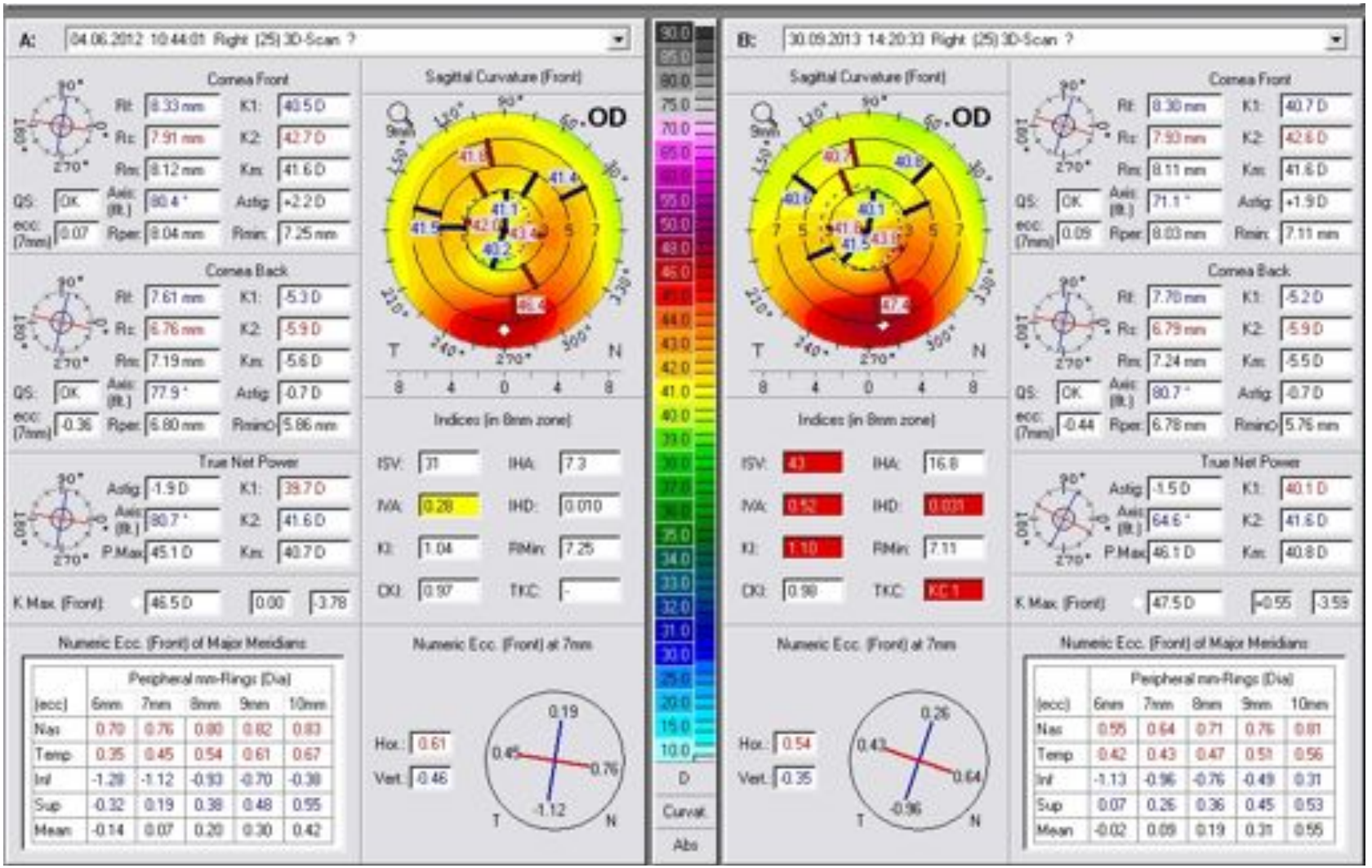
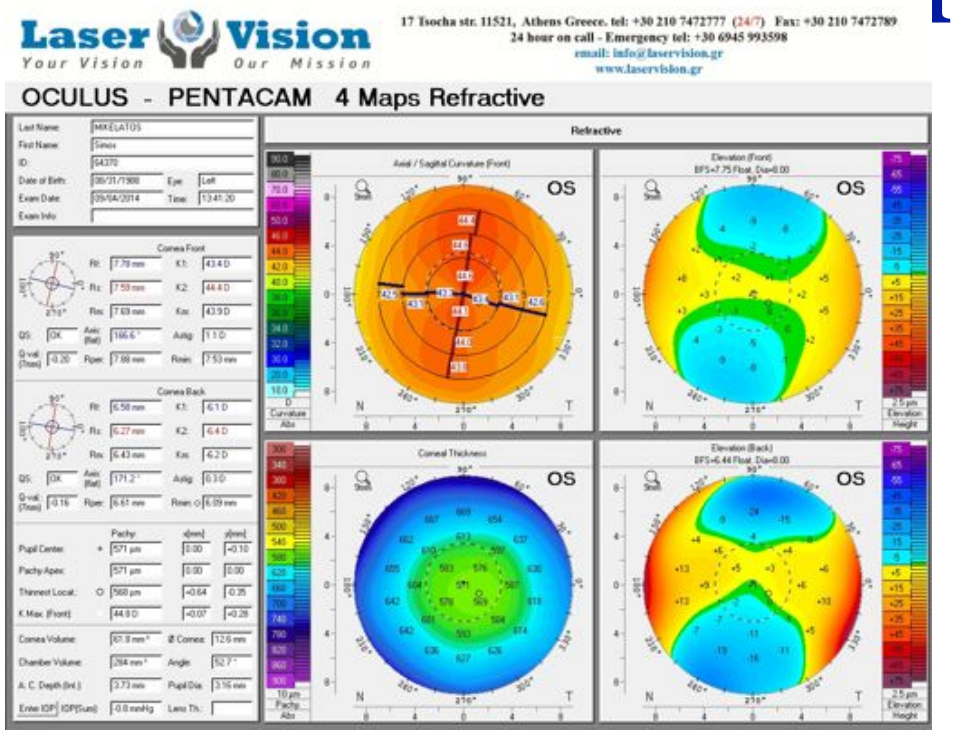
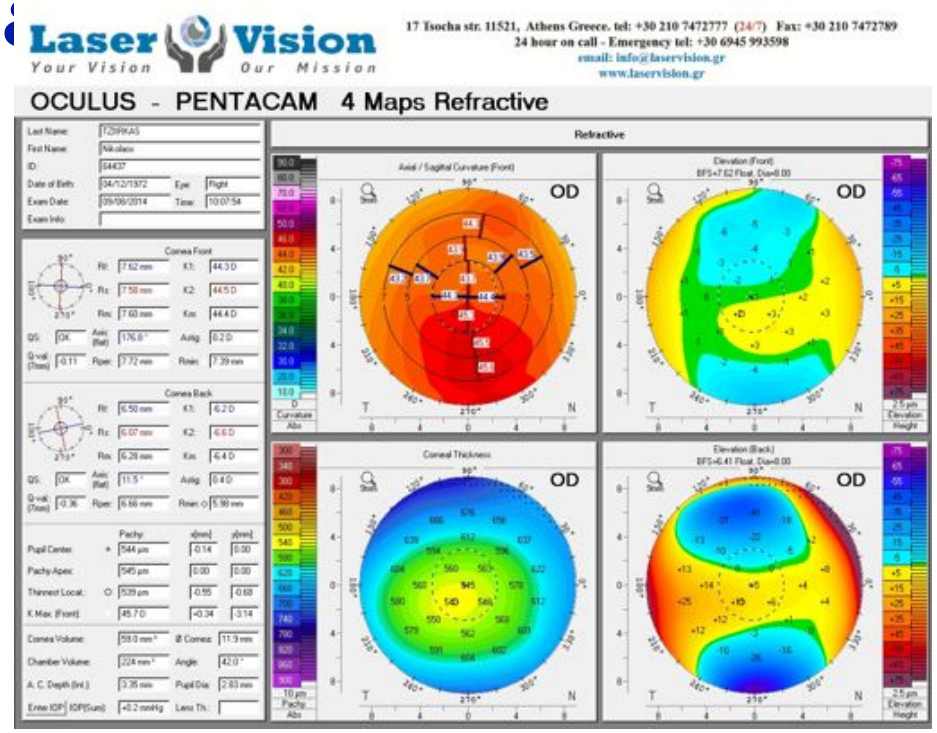

A: 04.06.2012 10:44:01 Right (25) 3D-Scan ?
Cornea Front
Cornea Back
True Net Power
Sagittal Curvature (Front)
.OD
Indices (in 8mm zone)
K Max (Front): 46.5 D
Numeric Ecc. (Front) of Major Meridians
Peripheral mm-Rings (Dia)
Numeric Ecc. (Front) at 7mm
B: 30.09.2013 14:20:33 Right (25) 3D-Scan ?
Cornea Front
Cornea Back
True Net Power
Sagittal Curvature (Front)
.OD
Indices (in 8mm zone)
K Max (Front): 47.5 D
Numeric Ecc. (Front) of Major Meridians
Peripheral mm-Rings (Dia)
Numeric Ecc. (Front) at 7mm

Qualitative pachymetry changes





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ORIGINAL RESEARCH

Revisiting keratoconus diagnosis and progression classification based on evaluation of corneal asymmetry indices, derived from Scheimpflug imaging in keratoconic and suspect cases

Anastasios John Kanellopoulos[1,2]
George Asimellis[1]

[1]Laservision.gr Eye Institute, Athens, Greece; [2]New York University School of Medicine, New York, NY, USA

Purpose: To survey the standard keratoconus grading scale (Pentacam®-derived Amsler–Krumeich stages) compared to corneal irregularity indices and best spectacle-corrected distance visual acuity (CDVA).

Patients and methods: Two-hundred and twelve keratoconus cases were evaluated for keratoconus grading, anterior surface irregularity indices (measured by Pentacam imaging), and subjective refraction (measured by CDVA). The correlations between CDVA, keratometry, and the Scheimpflug keratoconus grading and the seven anterior surface Pentacam-derived topometric indices – index of surface variance, index of vertical asymmetry, keratoconus index, central keratoconus index, index of height asymmetry, index of height decentration, and index of minimum radius of curvature – were analyzed using paired two-tailed *t*-tests, coefficient of determination (r^2), and trendline linearity.

Results: The average ± standard deviation CDVA (expressed decimally) was 0.626 ± 0.244 for all eyes (range 0.10–1.00). The average flat meridian keratometry was (K1) 46.7 ± 5.89 D; the average steep keratometry (K2) was 51.05 ± 6.59 D. The index of surface variance and the index of height decentration had the strongest correlation with topographic keratoconus grading ($P < 0.001$). CDVA and keratometry correlated poorly with keratoconus severity.

Conclusion: It is reported here for the first time that the index of surface variance and the index of height decentration may be the most sensitive and specific criteria in the diagnosis, progression, and surgical follow-up of keratoconus. The classification proposed herein may present a novel benchmark in clinical work and future studies.

Keywords: diagnosis and classification, Pentacam topometric indices, Amsler–Krumeich keratoconus grading, surface variance, vertical asymmetry, keratoconus index, central keratoconus index, height asymmetry, height decentration, minimum radius of curvature

Video abstract

Point your SmartPhone at the code above. If you have a QR code reader the video abstract will appear. Or use: http://dvpr.es/11vcPjX

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Introduction

Keratoconus is described as a degenerative bilateral, progressive, noninflammatory corneal disorder characterized by ectasia, thinning, and increased curvature.[1,2] It is associated with loss of visual acuity particularly in relation to progressive cornea irregularity,[3,4] and usually is manifested asymmetrically between the two eyes of the same patient.[5,6] Occasionally, the patient may present with symptoms of photophobia, glare, and monocular diplopia.

The problem of specificity and sensitivity of keratoconus assessment, particularly the diagnosis of early signs of ectasia and/or subclinical keratoconus, and for monitoring the progression of the disease, has been extensively studied.[7] The commonly used

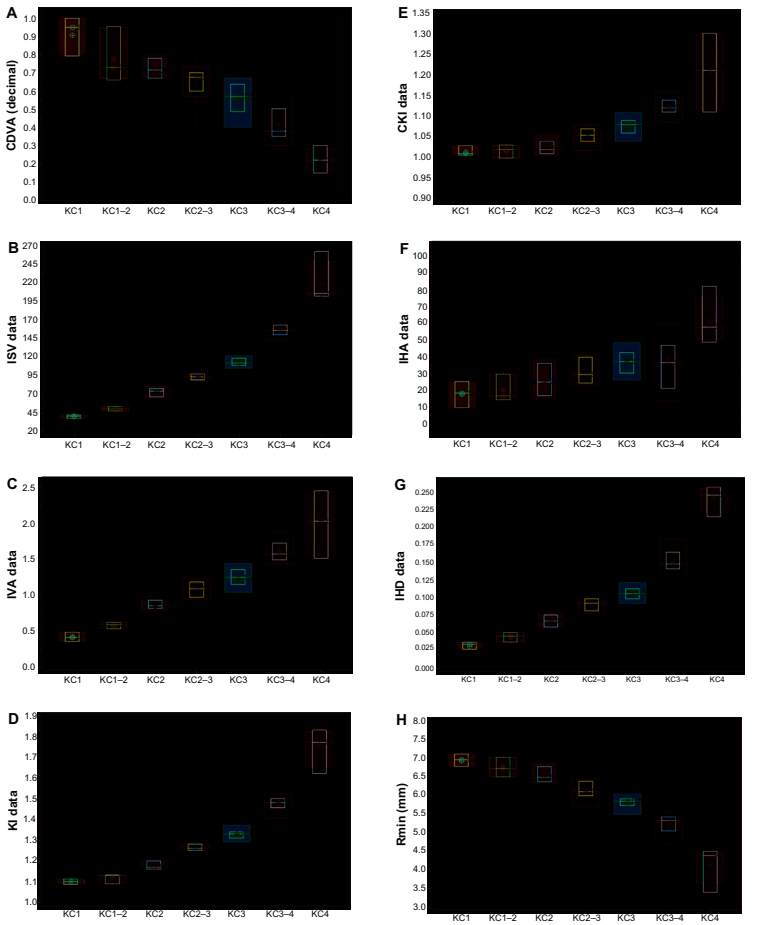

Figure 2 Box plots of measured parameters versus keratoconus grading, as produced by the Oculyzer™ software, showing median level (indicated by □), average symbol (□), 95% median confidence range box (black line boxes), and interquartile intervals range box (red line boxes). (**A**) CDVA versus keratoconus grading. (**B**) ISV versus keratoconus grading. (**C**) IVA versus keratoconus grading. (**D**) KI versus keratoconus grading. (**E**) CKI versus keratoconus. (**F**) IHA versus keratoconus grading. (**G**) IHD versus keratoconus grading. (**H**) Rmin versus keratoconus grading.
Abbreviations: CDVA, best spectacle-corrected distance visual acuity; CKI, central keratoconus index; IHA, index of height asymmetry; IHD, index of height decentration; ISV, index of surface variance; IVA, index of vertical asymmetry; KC1, keratoconus grading Stage I; KC1–2, keratoconus grading Stage I–II; KC2, keratoconus grading Stage II, KC2–3, keratoconus grading Stage II–III; KC3, keratoconus grading Stage III; KC3–4, keratoconus grading Stage III–IV; KC4, keratoconus grading Stage IV; KI, keratoconus index; PI, prediction interval; Rmin, minimum radius of curvature.

10.5005/jp-journals-10025-1060

ORIGINAL ARTICLE

Evaluation of Visual Acuity, Pachymetry and Anterior-Surface Irregularity in Keratoconus and Crosslinking Intervention Follow-up in 737 Cases

Anastasios John Kanellopoulos, Vasiliki Moustou, George Asimellis

ABSTRACT

Purpose: To investigate visual acuity, corneal pachymetry, and anterior-surface irregularity indices correlation with keratoconus severity in a very large pool of clinically-diagnosed untreated keratoconic eyes, and in keratoconic eyes subjected to cross-linking intervention.

Materials and methods: Total of 737 keratoconic (KCN) cases were evaluated. Group A was formed from 362 untreated keratoconic eyes, and group B from 375 keratoconic eyes subjected to partial normalization via topography-guided excimer laser ablation and high-fluence collagen crosslinking. A control group C of 145 healthy eyes was employed for comparison. We investigated distance visual acuity, uncorrected (UDVA), best-spectacle corrected (CDVA), and Scheimpflug-derived keratometry, pachymetry (central corneal thickness, CCT and thinnest, TCT), and two anterior-surface irregularity indices, the index of surface variance (ISV) and the index of height decentration (IHD). The correlations between these parameters *vs* topographic keratoconus classification (TKC) were investigated.

Results: Keratometry for group A was K1 (flat) 46.67 ± 3.80 D and K2 (steep) 50.76 ± 5.02 D; for group B K1 44.03 ± 3.64 D and K2 46.87 ± 4.61 D; for group C, K1 42.89 ± 1.45 D and K2 44.18 ± 1.88 D. Visual acuity for group A was UDVA 0.12 ± 0.18 and CDVA 0.59 ± 0.25 (decimal), for group B, 0.51 ± 0.28 and 0.77 ± 0.22, and for group C, 0.81 ± 0.31 and 0.87 ± 0.12.

Correlation between ISV and TKC (r^2) was for group A 0.853, and for group-B 0.886. Correlation between IHD and TKC was for group A $r^2 = 0.731$, and for group B 0.701. The ROC analysis 'area under the curve' was for CDVA 0.550, TCT 0.596, ISV 0.876 and IHD 0.887.

Conclusion: Our study indicates that the traditionally employed metrics of visual acuity and corneal thickness may not be robust indicators nor provide accurate assessment on either keratoconus severity or postoperative evaluation. Two anterior surface irregularity indices, derived by Scheimpflug-imaging, ISV and IHD, may be more sensitive and specific tools.

Précis: Visual acuity, Scheimpflug-derived pachymetry and anterior-surface irregularity correlation to keratoconus severity in untreated cases (A), treated with crosslinking (B), and in a control group (C) reveals that visual acuity and pachymetry do not correlate well with keratoconus severity.

Keywords: Athens Protocol, Combined topography guided PRK and higher fluence CXL, Visual rehabilitation in keratoconus, Severity criteria, Keratoconus progression, Keratoconus classification, Pentacam, Keratoconic Scheimpflug topometric indices, Visual acuity, Keratoconus, Grading anterior surface Pentacam indices, Keratoconus Amsler and Krumeich grading, Corneal pachymetry, Receiver operating characteristic ROC analysis.

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Source of support: Nil

Conflict of interest: None declared

INTRODUCTION

Keratoconus (KCN), derived from the Greek words κερατοειδής: cornea; κώνος: cone, meaning cone-shaped protrusion, is a corneal disorder, defined as a noninflammatory degenerative axial thinning of an ectatic cornea.[1] Vision is affected by increased myopia due to the cone protrusion, and irregular astigmatism due to substantial corneal asymmetry.[2-4]

Our long clinical experience with keratoconic screening and rehabilitation[5-7] indicates that neither corneal pachymetry nor visual acuity (uncorrected distance visual acuity, UDVA, and best-spectacle corrected distance visual acuity, CDVA) can be reliable indicators of ectasia and/or keratoconus progression assessment.[8] One may expect that the presence of large amounts of corneal irregularities might hamper sufficient spectacle-correction of visual acuity. However, at least in our experience, often enough keratoconic patients present with surprisingly high CDVA, even near 20/20, despite severe topographic irregularity and/or pachymetric thinning present. This makes keratoconus diagnosis a difficult and potentially dangerous process, as most early, many advanced and even some severe cases can be missed with traditional screening methods. We have also encountered cases with progressive keratoconus with no clinically significant reduction in visual acuity.

To the best of our knowledge, the subject of quantitative correlation of visual acuity with keratoconus grading[9-11] has been reported only in very few peer-review publications.

This study aims to investigate the possible correlations of visual acuity (UDVA and CDVA), corneal pachymetry, and specific Scheimpflug-imaging derived anterior-surface topographic irregularity indices with keratoconus severity, in a large pool of clinically-diagnosed keratoconic eyes, and in a group of keratoconic eyes subjected to cross-linking and anterior-surface normalization intervention, and examine the applicability of these indicators in keratoconus screening,

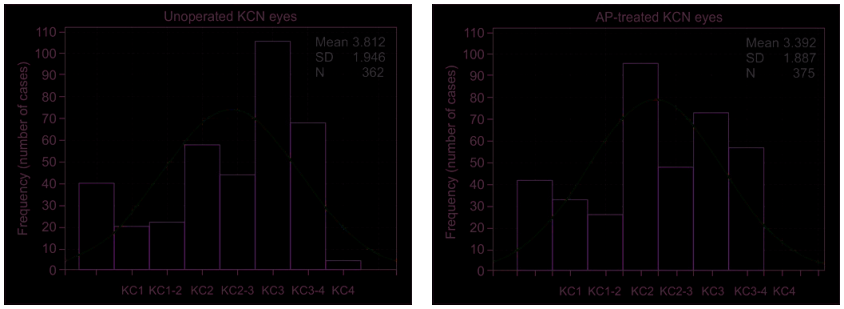


Fig. 1: Histograms of keratoconus classification for the two groups under study. Left — group A, unoperated KCN eyes and, right — group B, Athens-protocol (AP) treated KCN eyes

Table 2: Coefficient of determination (r^2) and pearson correlation coefficient for the two groups in the study between UDVA and TKC, CDVA and TKC, TCT and TKC, ISV TKC, IHD and TKC

	Coefficient of determination (r^2)	*Pearson correlation coefficient*
UDVA vs TKC		
Group A, unoperated KCN eyes	0.071	– 2.931
Group B, AP-treated KCN eyes	0.263	– 3.367
CDVA vs TKC		
Group A, unoperated KCN eyes	0.292	– 4.285
Group B, AP-treated KCN eyes	0.175	– 3.549
TCT vs TKC		
Group A, unoperated KCN eyes	0.236	– 0.0245
Group B, AP-treated KCN eyes	0.176	– 0.0131
ISV vs TKC		
Group A, unoperated KCN eyes	0.853	0.0415
Group B, AP-treated KCN eyes	0.886	0.0485
IHD vs TKC		
Group A, unoperated KCN eyes	0.731	31.9
Group B, AP-treated KCN eyes	0.701	43.1

KCN: keratoconus; UDVA: uncorrected distance visual acuity (decimal); TKC: topographic keratoconus classification; CDVA: best-spectacle corrected distance visual acuity (units, decimal); TCT: thinnest corneal thickness (units, μm); ISV: index of surface variance; IHD: index of height decentration; AP: Athens-protocol

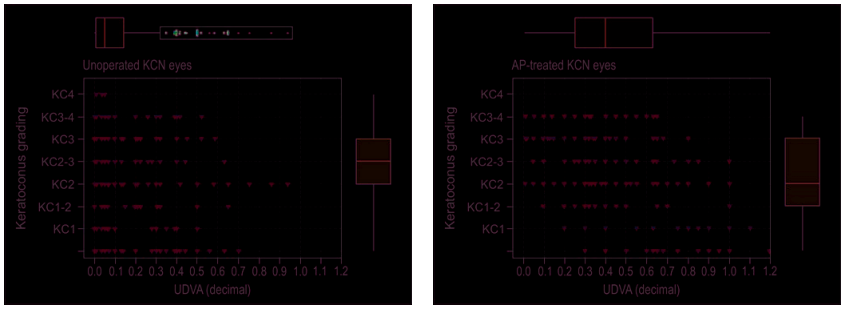
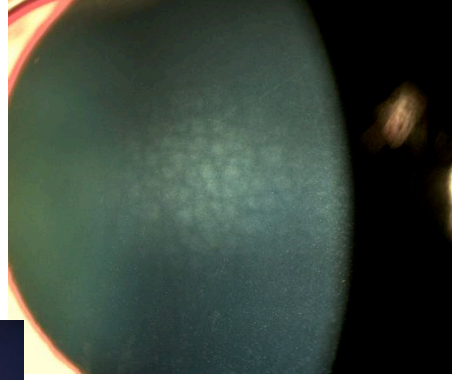
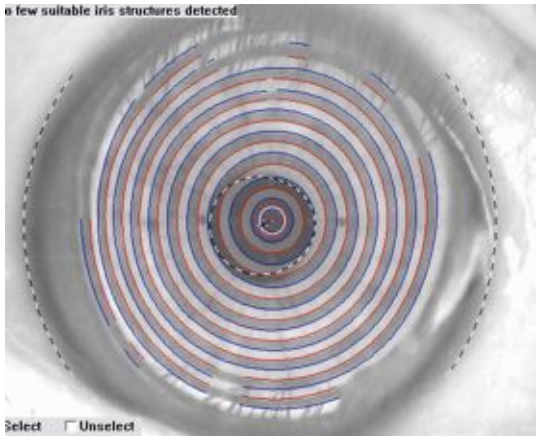


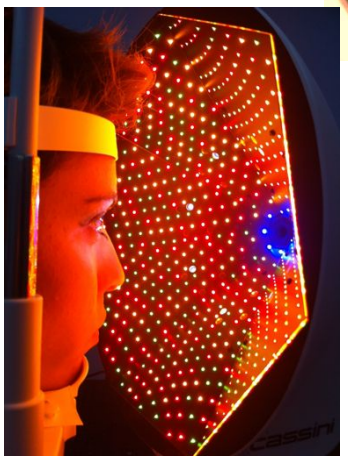
Fig. 2: Marginal plot of UDVA (expressed decimally) and TKC grading with overlying box plots showing mean levels and outliers. Left — group A, unoperated KCN eyes and, right — group B, Athens-protocol (AP) treated KCN eyes

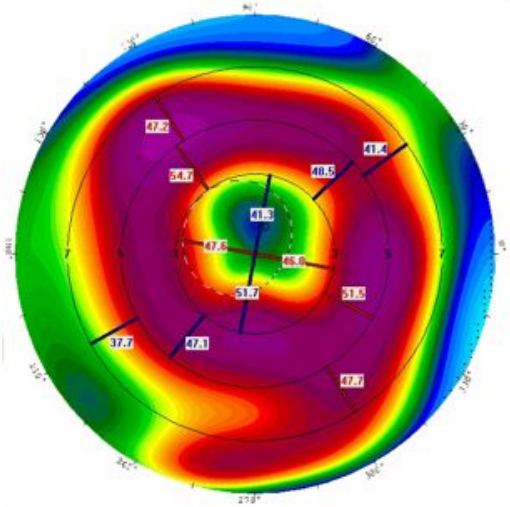
A simple case of Central Cloudy dystrophy (Francois) illustrates the possible discrepancy between different imaging modalities

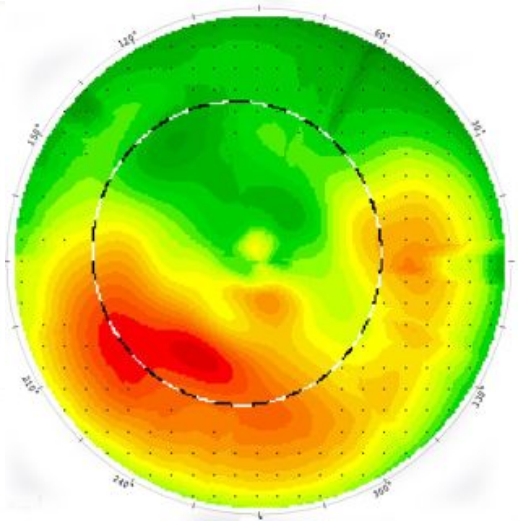
Kanellopoulos AJ, Asimellis G CRO 2013

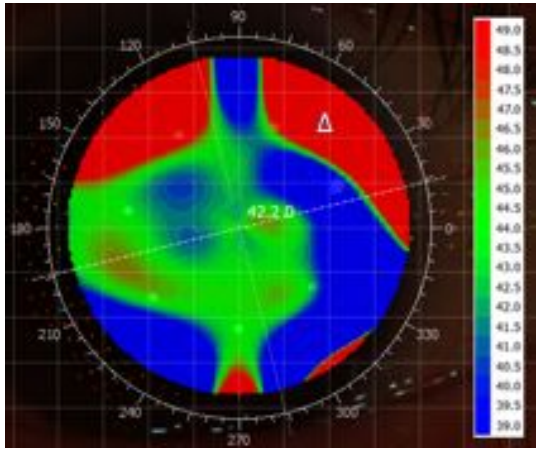












In Vivo Three-Dimensional Corneal Epithelium Imaging in Normal Eyes by Anterior-Segment Optical Coherence Tomography: A Clinical Reference Study

Anastasios John Kanellopoulos, MD,† and George Asimellis, PhD**

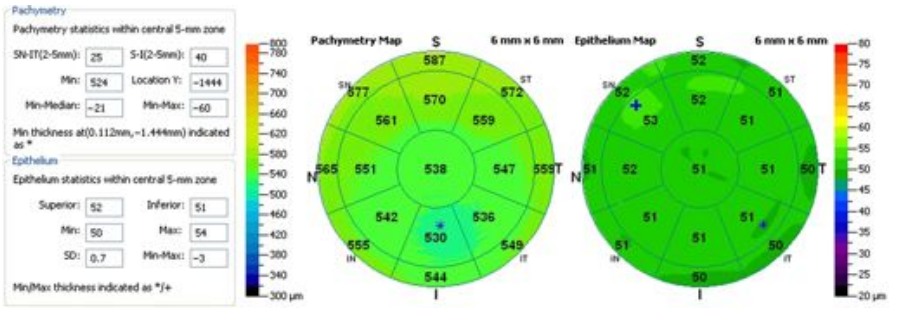


FIGURE 1. Details from the analysis software main report, showing corneal and epithelial 3-dimensional pachymetry maps over the 6-mm corneal diameter. The symbol * indicates the thickness minimum (both corneal and epithelial maps), and the symbol + indicates the thickness maximum (epithelial map only).

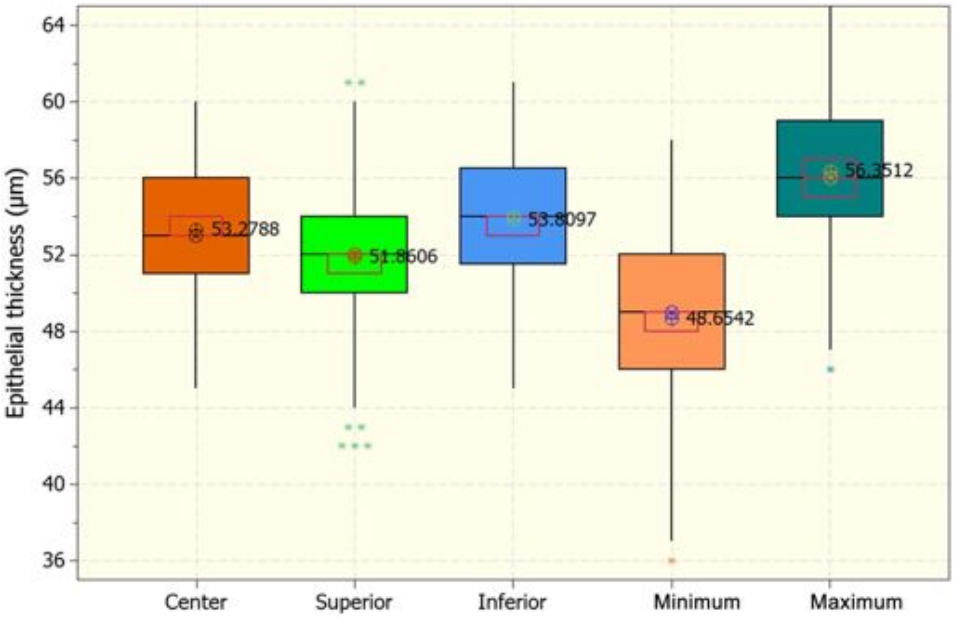


FIGURE 2. Box plot describing central, superior, inferior, minimum, and maximum epithelial thickness for all 373 cases. The median level is displayed numerically and indicated by ⊗, average by ⊕, the 95% median confidence range box by the red borderline, and the interquartile intervals range box by the black borderline. All units are in micrometers.

In Vivo 3-Dimensional Corneal Epithelial Thickness Mapping as an Indicator of Dry Eye: Preliminary Clinical Assessment

ANASTASIOS JOHN KANELLOPOULOS AND GEORGE ASIMELLIS

- PURPOSE: **To evaluate in vivo epithelial thickness in dry eye by anterior segment optical coherence tomography.**
- DESIGN: **Observational, retrospective case-control study.**
- METHODS: **Two age-matched groups of female subjects, 70 eyes each, age ≈ 55 years, were studied in clinical practice setting: a control (unoperated, no ocular pathology) and a dry eye group (clinically confirmed dry eye, unoperated and no other ocular pathology). Corneal epithelium over the entire cornea was topographically imaged via a novel anterior segment optical coherence tomography (AS-OCT) system. Average, central, and peripheral epithelial thickness as well as topographic epithelial thickness variability were measured.**
- RESULTS: **For the control group, central epithelial thickness was 53.0 ± 2.7 μm (45-59 μm). Average epithelium thickness was 53.3 ± 2.7 μm (46.7-59.6 μm). Topographic thickness variability was 1.9 ± 1.1 μm (0.7-6.1 μm). For the dry eye group, central epithelial thickness was 59.5 ± 4.2 μm (50-72 μm) and average thickness was 59.3 ± 3.4 μm (51.4-70.5 μm). Topographic thickness variability was 2.5 ± 1.5 μm (0.9-6.9 μm). All pair tests of respective epithelium thickness metrics between the control and dry eye group show statistically significant difference ($P < .05$).**
- CONCLUSIONS: **This study, based on very user-friendly, novel AS-OCT imaging, indicates increased epithelial thickness in dry eyes. The ease of use and the improved predictability offered by AS-OCT epithelial imaging may be a significant clinical advantage. Augmented epithelial thickness in the suspect cases may be employed as an objective clinical indicator of dry eye.** (Am J Ophthalmol 2014;157:63–68. © 2014 by Elsevier Inc. All rights reserved.)

DRY EYE IS A MULTIFACTORIAL DISEASE OF THE tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface.[1]

Dry eye is responsible for significant population morbidity and is a common clinical problem for eye clinicians. Besides the significant symptoms and toll on quality of life, it may present significant challenges in refractive surgery patient assessment.[2] As reported in the peer-review literature,[3–7] its manifestations may range from episodic and mild condition to chronic and severe disease: the disorder can be presented with any or many symptoms of visual disturbance and blurred vision, eye discomfort, irritation, foreign body sensation, ocular surface damage, redness, excess tearing, and photosensitivity.

Epidemiologic review studies estimate the prevalence of dry eye disease between 4% and 33%, largely depending, among other factors, on the diagnosis mode, the geographic locale,[8,9] age, and sex, being most prominent in the middle-aged (over age 45 years) female populace.[10–12]

Several clinically available modalities may facilitate in vivo measurement of corneal epithelium, including high-frequency scanning ultrasound biomicroscopy (HF-UBM),[13] anterior segment optical coherence tomography (AS-OCT),[14] and confocal microscopy through focusing (CMTF).[15,16] In the clinical practice, epithelial evaluation is limited by the resolution and the variability of the ocular surface tests.[17]

In pursuit of an objective, repeatable, and quantitative clinical test that may aid in the differential diagnosis of dry eye, we introduce the concept of corneal epithelial thickness as a possible tool in dry eye assessment. We report herein initial clinical results regarding 3-dimensional corneal epithelial thickness mapping in dry eye corneas with a newly commercially available anterior segment optical coherence tomography system.

MATERIALS AND METHODS

THIS OBSERVATIONAL, RETROSPECTIVE CASE-CONTROL study received approval by the Ethics Committee of our Institution (LaserVision.gr Eye Institute), and was adherent to the tenets of the Declaration of Helsinki. Written informed consent was obtained from each subject

Accepted for publication Aug 29, 2013.

From Laservision.gr Eye Institute, Athens, Greece (A.J.K., G.A.); and New York University Medical School, New York, New York (A.J.K.).

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http://dx.doi.org/10.1016/j.ajo.2013.08.025

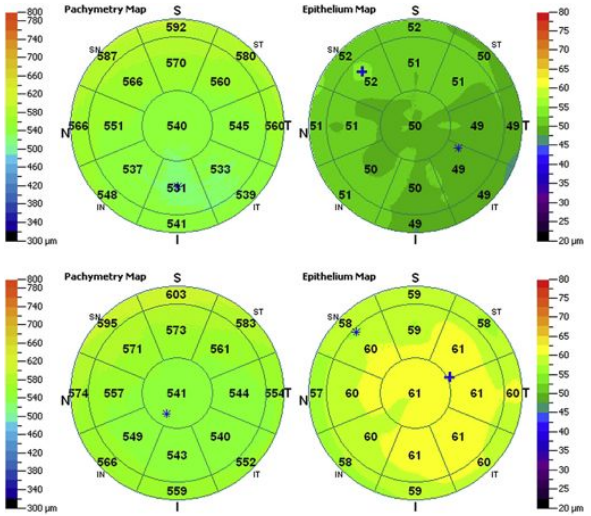

FIGURE 1. Representative corneal total thickness maps (left) and corneal epithelium thickness maps (right) of (Top) a "normal" patient from Group A and (Bottom) a dry eye patient from Group B, as provided by the optical coherence tomography system report.

DISCUSSION

THE CHALLENGE OF OBJECTIVE DRY EYE ASSESSMENT HAS been argued in length. The current options of the clinical investigator includes slit-lamp observations, osmolarity test, tear-film breakup time measurement, Schirmer lacrimation test, corneal and conjunctival staining, meibomian grading, and Ocular Surface Disease Index.[10] Research evidence suggests that clinical dry eye symptoms alone may be insufficient for the diagnosis and management of dry eye, and there is argument for a consensus of newer metrics that may better reflect the differential discrimination of the disease.[18]

One such possible element in diagnosis is overall epithelial thickness, as well as the topographic distribution of epithelial thickness. For example, atopic keratoconjunctivitis has been associated with significant alterations of the basal epithelium and subbasal and stromal corneal nerves, related to the changes in tear functions and corneal sensitivity.[19]

Very little is reported, however, in the peer-review literature on the subject matter of entire corneal area in vivo measurement of epithelial thickness, particularly in relationship with dry eye. This can be justified by the fact that neither HF-UBM nor AS-OCT nor CMTF techniques have been fully applicable and/or with a commercially available mode for this use, as well as the fact that some (eg, HF-UBM) employ instrument or fluid interface contact with the epithelium. We have not identified, for example, reported correlation of dry eye and HF-UBM measurements. CMTF has been restricted in this application because of the degraded precision by eye movement during the long acquisition time; in addition, other available clinical evaluation techniques for the corneal epithelium either are invasive or require contact between the probe and the ocular surface, and thus cannot provide precise in vivo measurement of the epithelial thickness.[20] In a confocal laser scanning microscopy study in dry eye,[21] the mean superficial and intermediate epithelial cell densities in the central cornea in the dry eye groups were significantly lower than in normal participants. Dry eye corneas showed significant alterations, presumably attributable to increased desquamation of the superficial cell layer.

Reports on entire corneal epithelium imaging via AS-OCT, a novel entity, have been also few. In most of these studies, investigator-modified software/hardware[22–24] or caliper software measurement techniques[25,26] have been employed (for example, by manually placing cursors to measure epithelial thickness in each location).

The recent availability of full-cornea corneal epithelial thickness imaging by AS-OCT potentially presents a practical clinical tool for qualitative (by examination of the

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ORIGINAL RESEARCH

Correlation between epithelial thickness in normal corneas, untreated ectatic corneas, and ectatic corneas previously treated with CXL; is overall epithelial thickness a very early ectasia prognostic factor?

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Video abstract

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Purpose: To determine and correlate epithelial corneal thickness (pachymetric) measurements taken with a digital arc scanning very high frequency ultrasound biomicroscopy (HF UBM) imaging system (Artemis-II), and compare mean and central epithelial thickness among normal eyes, untreated keratoconic eyes, and keratoconic eyes previously treated with collagen crosslinking (CXL).

Methods: Epithelial pachymetry measurements (topographic mapping) were conducted on 100 subjects via HF UBM. Three groups of patients were included: patients with normal eyes (controls), patients with untreated keratoconic eyes, and patients with keratoconic eyes treated with CXL. Central, mean, and peripheral corneal epithelial thickness was examined for each group, and a statistical study was conducted.

Results: Mean, central, and peripheral corneal epithelial thickness was compared between the three groups of patients. Epithelium thickness varied substantially in the keratoconic group, and in some cases there was a difference of up to 20 µm between various points of the same eye, and often a thinner epithelium coincided with a thinner cornea. However, on average, data from the keratoconic group suggested an overall thickening of the epithelium, particularly over the pupil center of the order of +3 µm, while the mean epithelium thickness was on average +1.1 µm, compared to the control population ($P = 0.005$). This overall thickening was more pronounced in younger patients in the keratoconic group. Keratoconic eyes previously treated with CXL showed, on average, virtually the same average epithelium thickness (mean −0.7 µm, −0.2 µm over the pupil center, −0.9 µm over the peripheral zone) as the control group. This finding further reinforces our novel theory of the "reactive" component of epithelial thickening in corneas that are biomechanically unstable, becoming stable when biomechanical rigidity is accomplished despite persistence of cornea topographic irregularity.

Conclusion: A highly irregular epithelium may be suggestive of an ectatic cornea. Our results indicate that the epithelium is thinner over the keratoconic protrusion, but to a much lesser extent than anticipated, and on average epithelium is thicker in this group of patients. This difference appears to be clinically significant and may become a screening tool for eyes suspected for ectasia.

Keywords: corneal pachymetry, ectasia, keratoconus screening, cornea epithelial thickness

Introduction

Importance of corneal epithelium imaging

The contribution of the corneal epithelium to the refractive power of the cornea, and thus ocular refraction, cannot be ignored. Studies have shown that epithelial refractive

- CXLed corneas has thinner epi
  - KCN corneas had OVERAL thicker epi
- Even suspect KCN corneas had THICKER epi

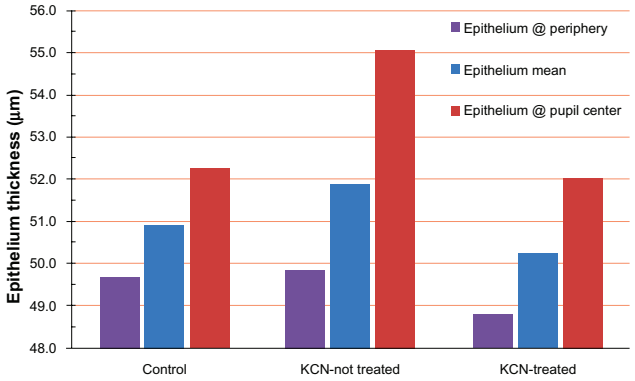

Figure 7 Epithelium thickness across the three study groups, at the periphery, mean, and pupil center.
Abbreviation: KCN, keratoconus.

surprise that while the epithelial center was, on average, thicker by only 1.3 µm compared to the mean, on several occasions it was thicker compared to the nasal, temporal, inferior, or superior points by up to 10 µm. This conclusion is also supported by the fact that the periphery epithelium thickness value of 49.7 µm was closer to the mean (50.9 µm) than to the pupil center (52.3 µm).

We note that the standard deviation of the measurements (±3–4 µm) is comparable to the accuracy and precision of the instrument, as established by our investigation, and thus epithelial thickness variations of ±4–4 µm, as it is the case, might be observed differently even on the same eye. An example of a control patient who demonstrated a thicker epithelium at the pupil center is shown in Figure 6. In one instance the central epithelium was elevated by 9 µm (51 µm–42 µm), while in a subsequent examination of the same eye, the difference between the same points was recorded as only 6 µm (54 µm–48 µm).

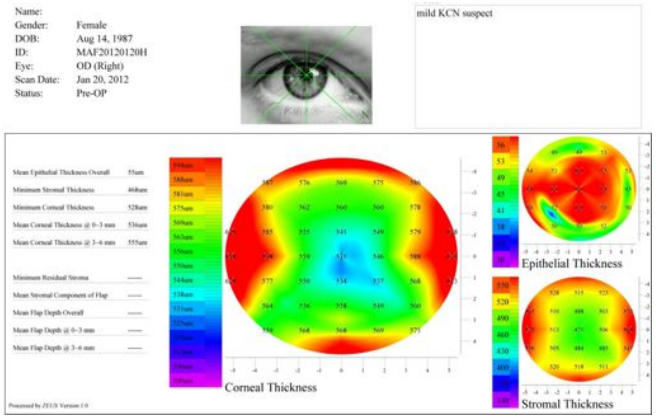

Figure 8 Corneal and epithelial thickness maps of a KCN patient.
Note: A significantly thicker epithelium over the pupil center is observed.
Abbreviation: KCN, keratoconus.

Epithelial remodeling after partial topography-guided normalization and high-fluence short-duration crosslinking (Athens protocol): Results up to 1 year

Anastasios John Kanellopoulos, MD, George Asimellis, PhD

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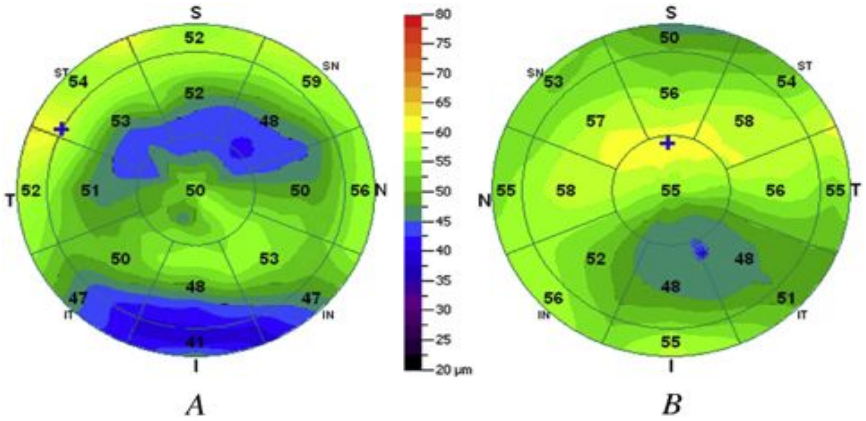

Figure 2. Comparative AS-OCT epithelial thickness (µm) 3-D maps shows an *i*mage from Group A taken 1 year postoperatively and an image from Group B (I = inferior; IN = inferior–nasal; IT = inferior–temporal; N = nasal; S = superior; SN = superior–nasal; ST = superior–temporal; T = temporal).

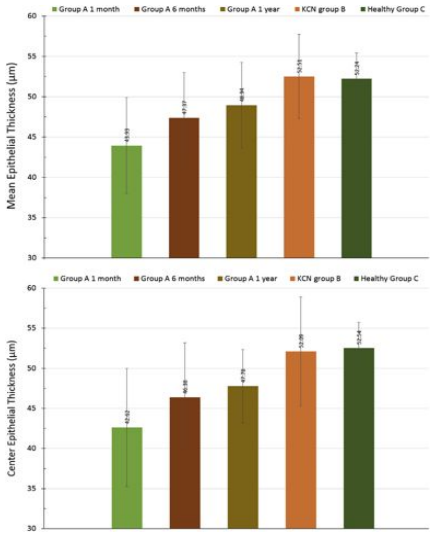

Figure 3. Mean and center epithelial thicknesses in the 3 groups. Error bars correspond to the SD (KCN = keratoconus, no treatment).

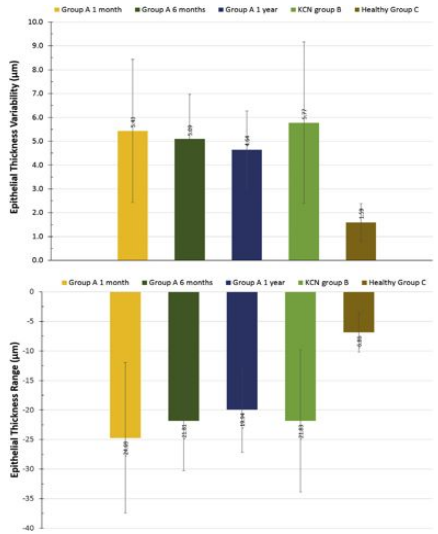

Figure 4. Epithelial thickness variability and range in the 3 groups. Error bars correspond to the SD (KCN = keratoconus, no treatment).

The findings in the current study agree with those in our previous study[1]; that is, although an overall thicker epithelium with large variations can be observed clinically and topographically in eyes with keratoconus, in eyes treated with CXL the variability in epithelium thickness and topographic thickness decreased by a statistically significant margin and was more uniform. We have theorized that epithelial hyperplasia in biomechanically unstable corneas (ie, increased epithelial regrowth activity) might be associated with a more elastic cornea.[1] The laboratory and clinical findings of increased corneal rigidity after CXL are widely accepted,[23–25] including in studies of accelerated high-fluence CXL.[26]

In conclusion, we present the results in a comprehensive study of the postoperative development of corneal epithelial thickness distribution after keratoconus management using combined anterior corneal normalization by topography-guided excimer ablation and accelerated CXL. The epithelial healing processes can be monitored by AS-OCT with ease in a clinical setting, expanding the clinical application of this technology. Our findings suggest less topographic variability and overall reduced epithelial thickness distribution in keratoconus eyes treated with CXL using the Athens protocol.

WHAT WAS KNOWN

- Postoperative epithelial remodeling after partial anterior surface normalization with an excimer laser and high-fluence CXL, assessed with high-frequency scanning UBM, results in reduced overall epithelial thickness and topographic variability.

WHAT THIS PAPER ADDS

- Detailed follow-up of Athens protocol–treated eyes up to 1 year confirmed previous ultrasound findings of the overall thinner and smoother epithelial thickness profiles compared with the profiles of untreated keratoconic eyes.

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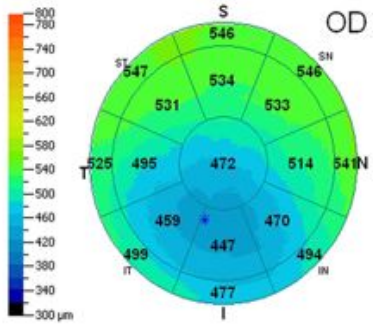
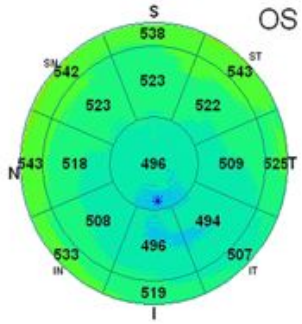
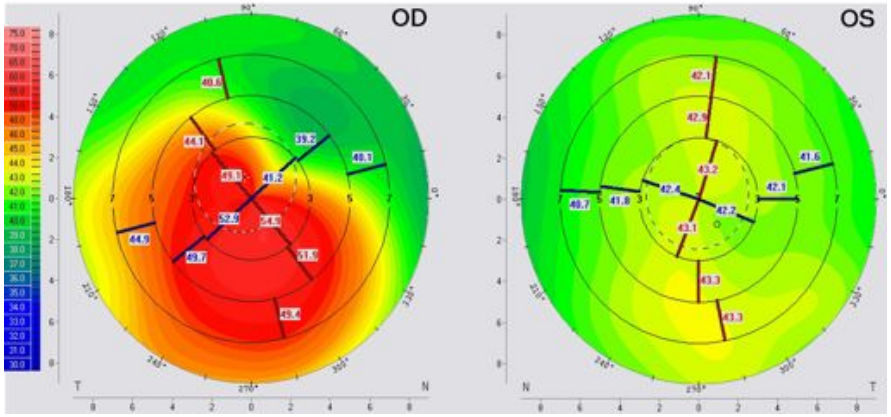
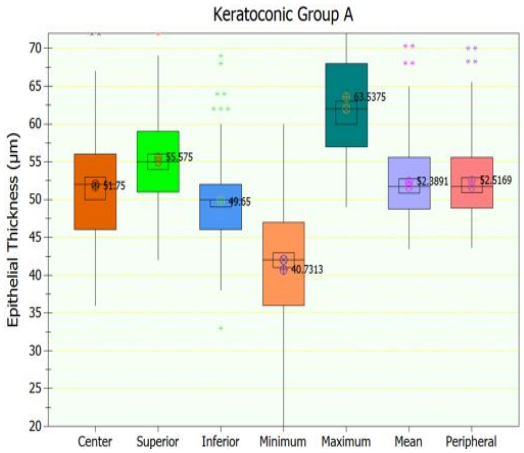
160 Normal Vs. 160 KCN epi distribution

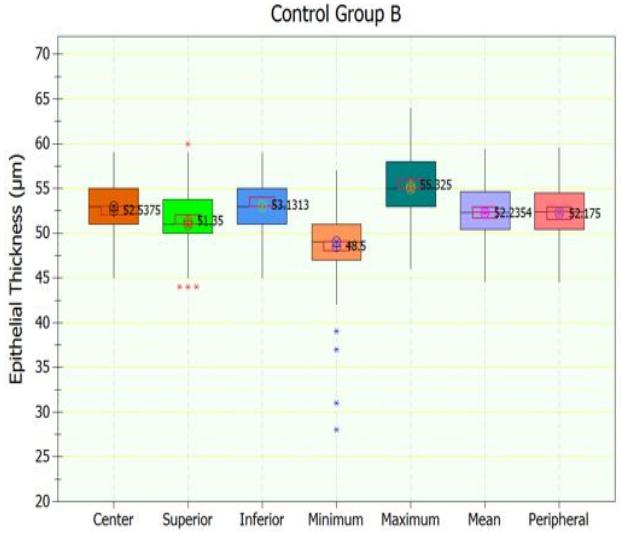






Box plots of epithelial thickness (showing center, superior, inferior, minimum, maximum, mean, and peripheral) showing median level (indicated by ⊗), average symbol (⊕), 95% median confidence and interquartile intervals range boxes. Top, keratoconic group-A, bottom, control group-B.





Optical coherence tomography–derived corneal thickness asymmetry indices: Clinical reference study of normal eyes

Anastasios John Kanellopoulos, MD, Marianthi Chiridou, OD, George Asimellis, PhD

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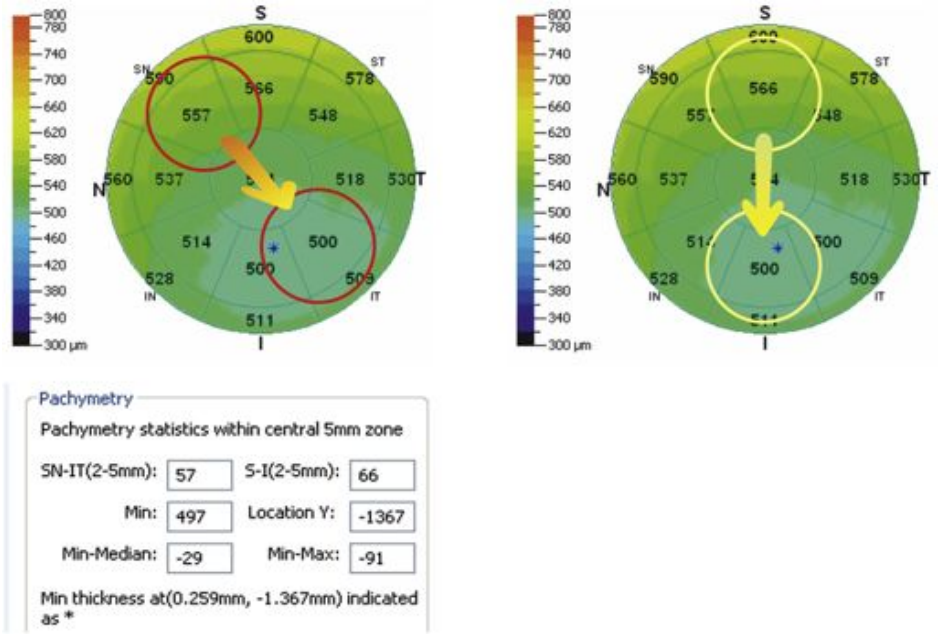


Figure 1. Definitions of SN–IT and S–I corneal asymmetry indices obtained by AS-OCT corneal 3-D pachymetry maps (6.0 mm diameter) (I = inferior; IN = inferonasal; IT = inferotemporal; Min-Max = thickness range, or global thinning, defined as the minimum corneal thickness minus the maximum corneal thickness; Min-Median = focal thinning, defined as the minimum corneal thickness minus the median corneal thickness; S = superior; S-I = superior–inferior; SN-IT = superonasal–inferotemporal; ST = superotemporal; T = temporal).

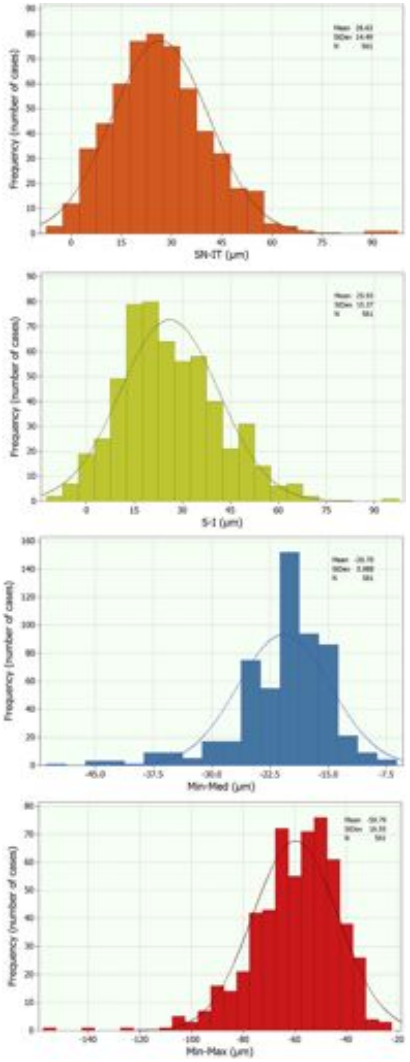
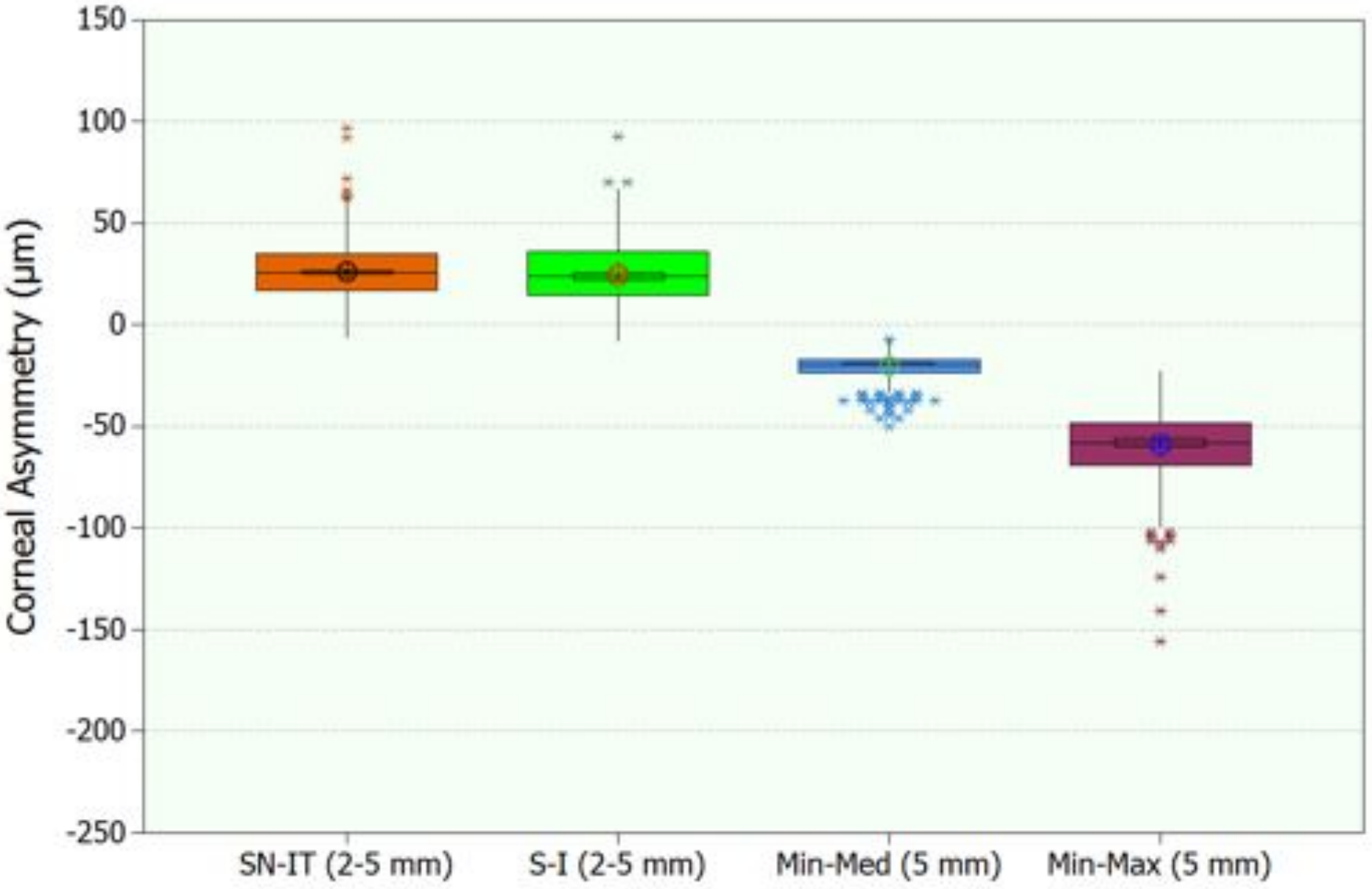
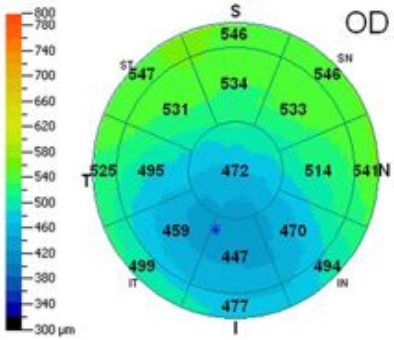


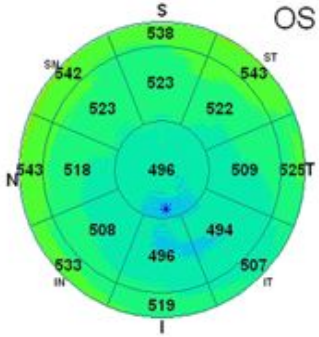
Figure 3. Optical coherence tomography–derived corneal asymmetry and thinning indices for the 561 cases (Min-Max = thickness range, or global thinning, defined as the minimum corneal thickness minus the maximum corneal thickness; Min-Med = focal thinning, defined as the minimum corneal thickness minus the median corneal thickness;

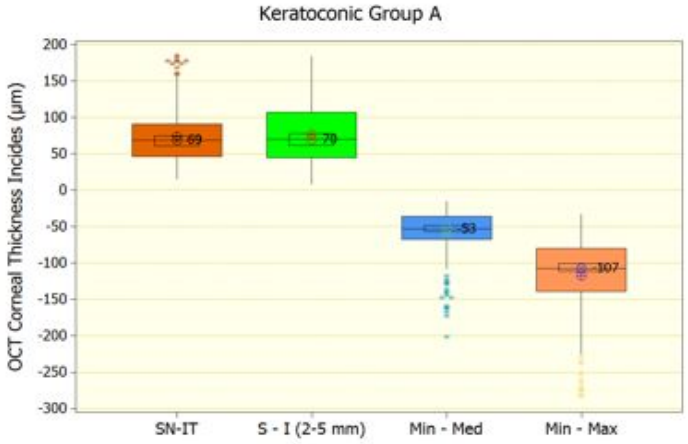

150
100
50
0
-50
-100
-150
-200
-250
Corneal Asymmetry (µm)
SN-IT (2-5 mm)
S-I (2-5 mm)
Min-Med (5 mm)
Min-Max (5 mm)

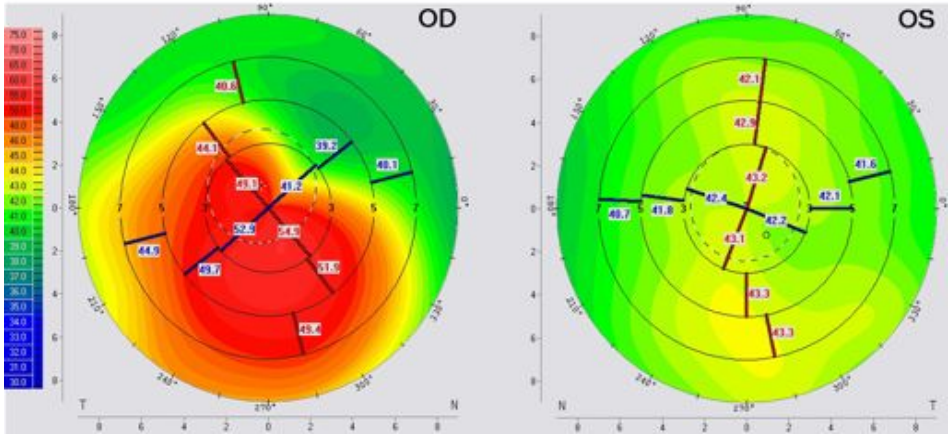
OCT-derived Comparison of Corneal Thickness Distribution and Asymmetry Differences between Normal (175) and Keratoconic Eyes(175)

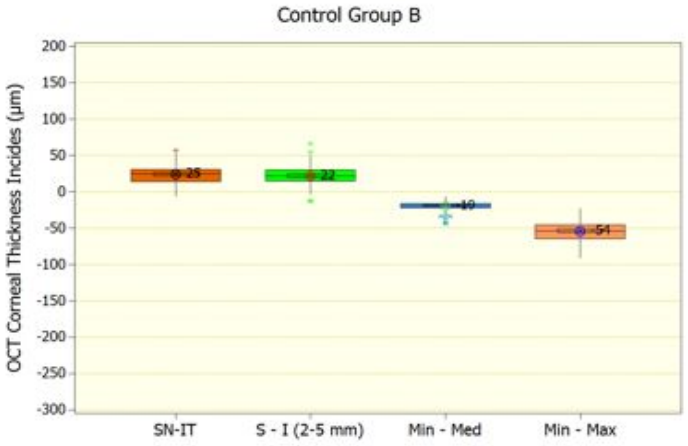
Kanellopoulos et al in press

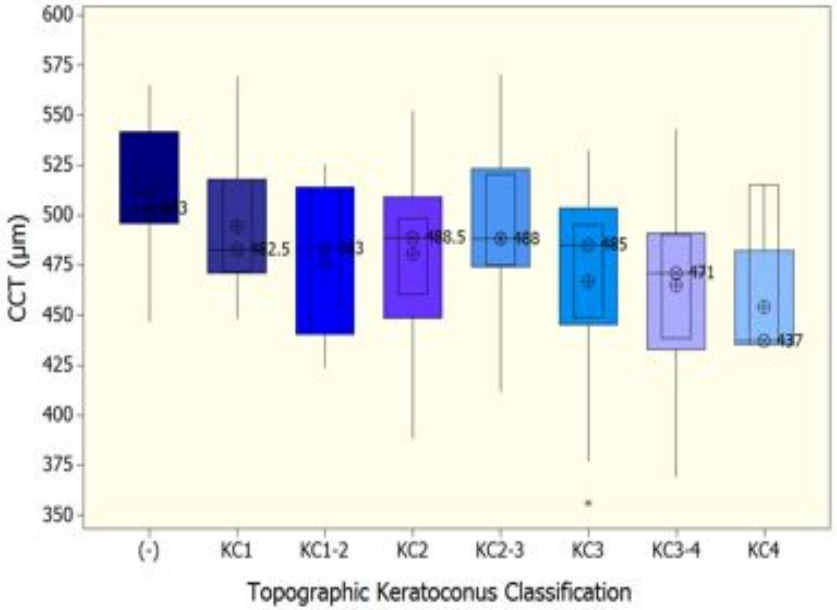


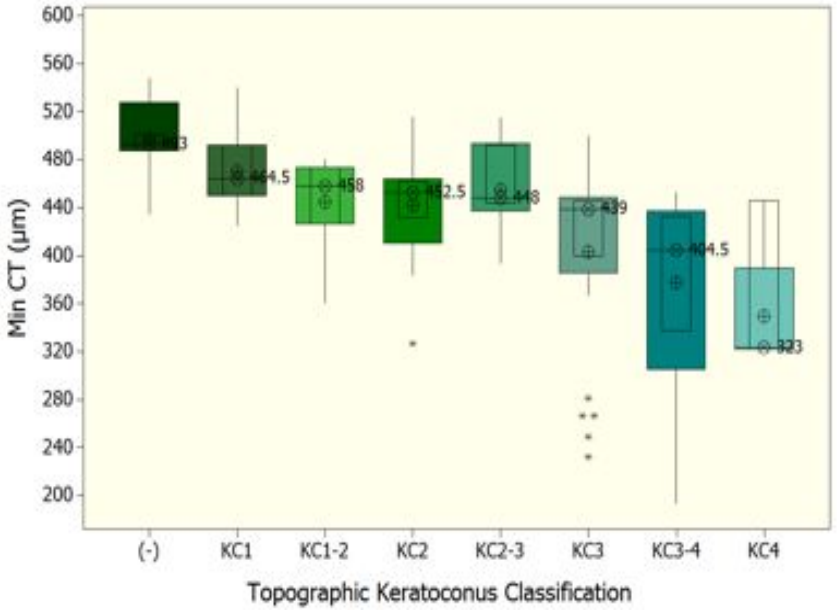


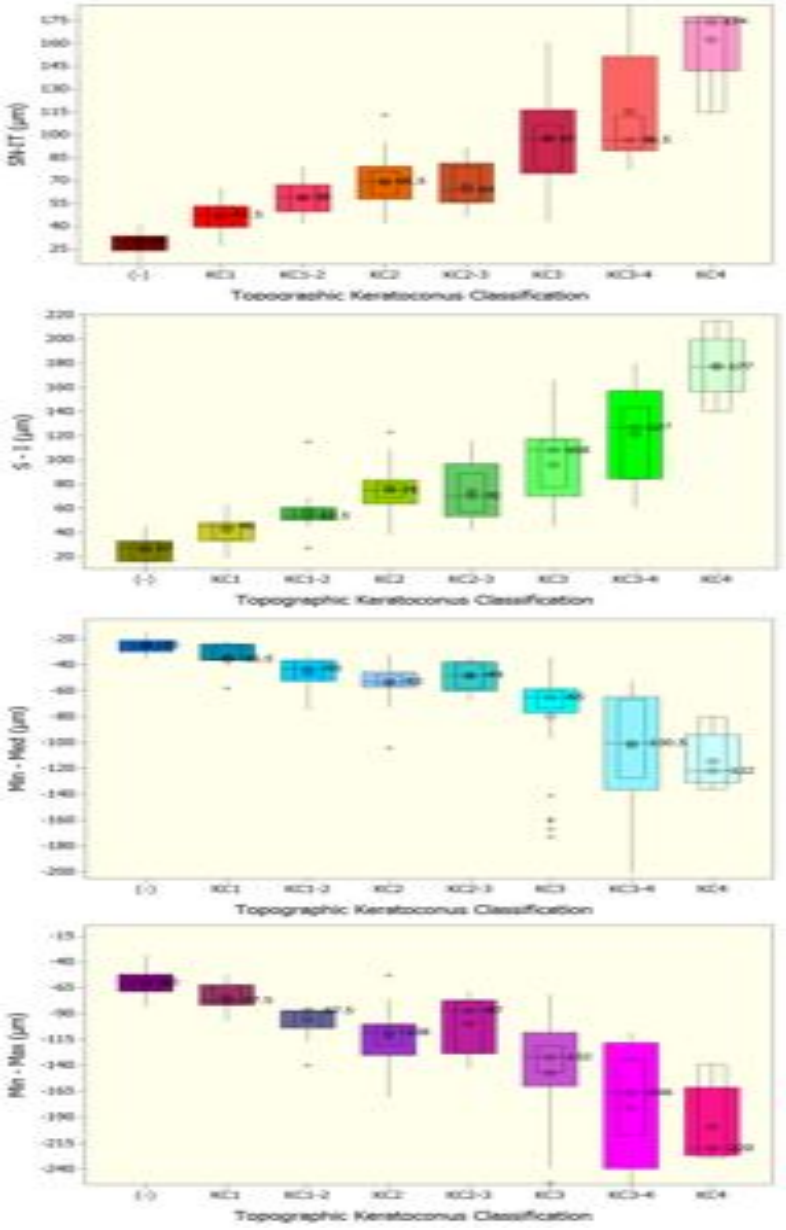












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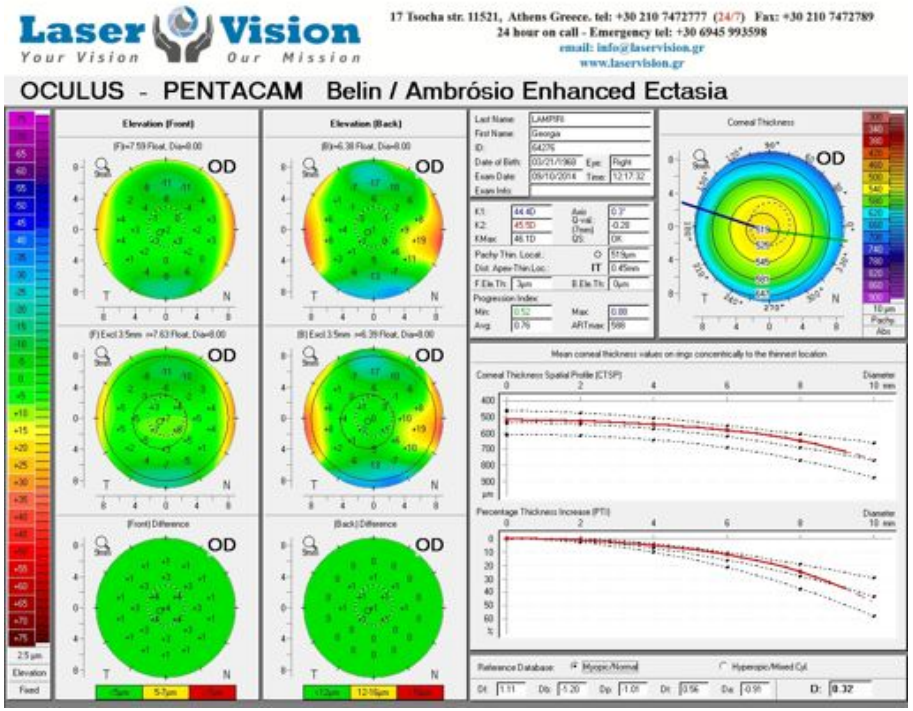

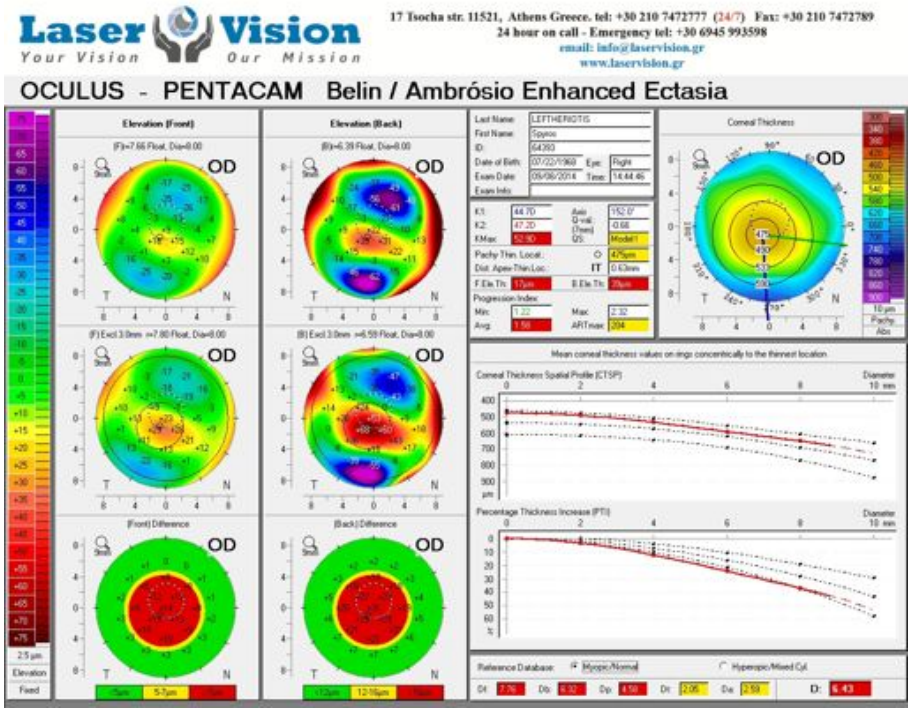

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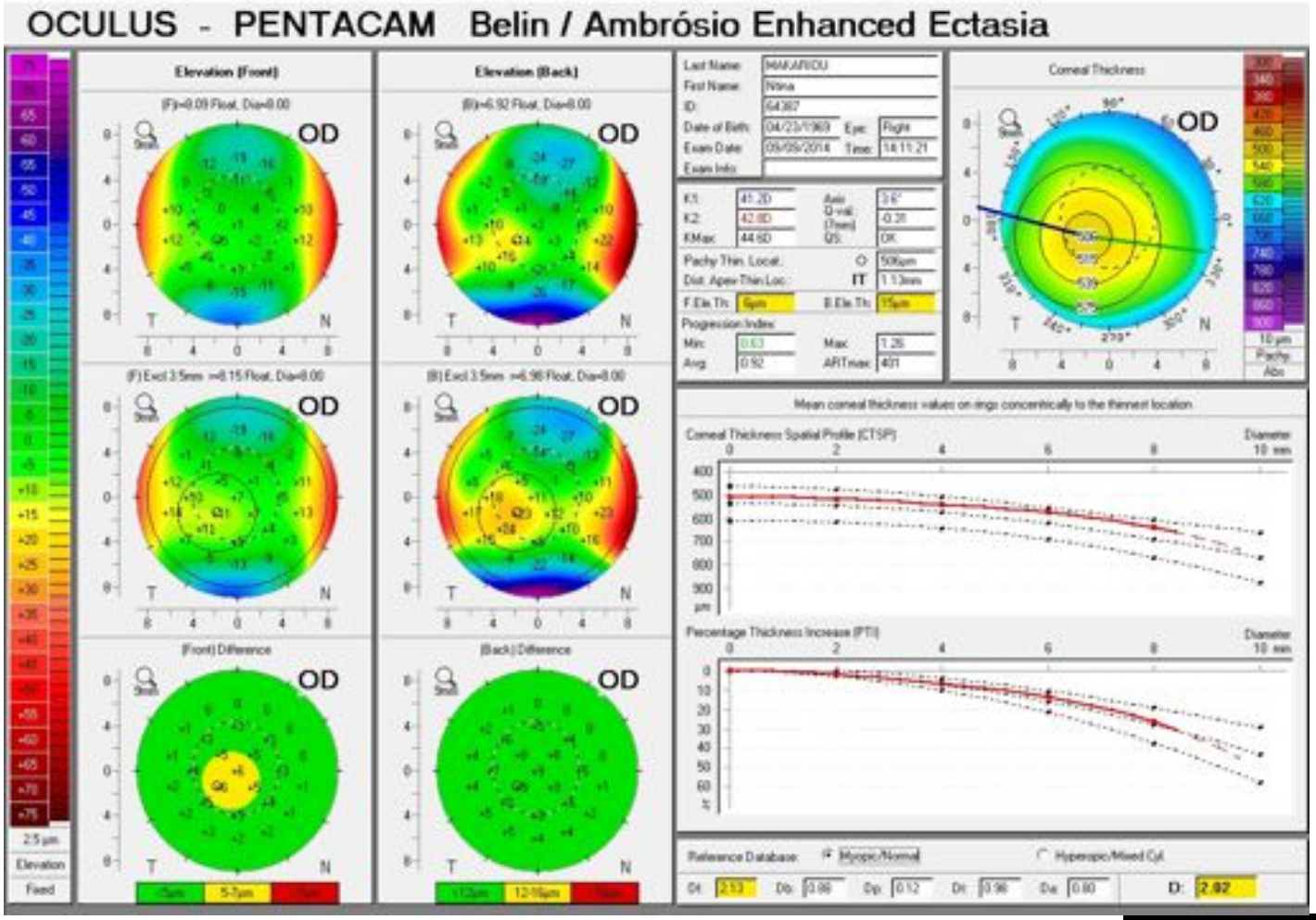

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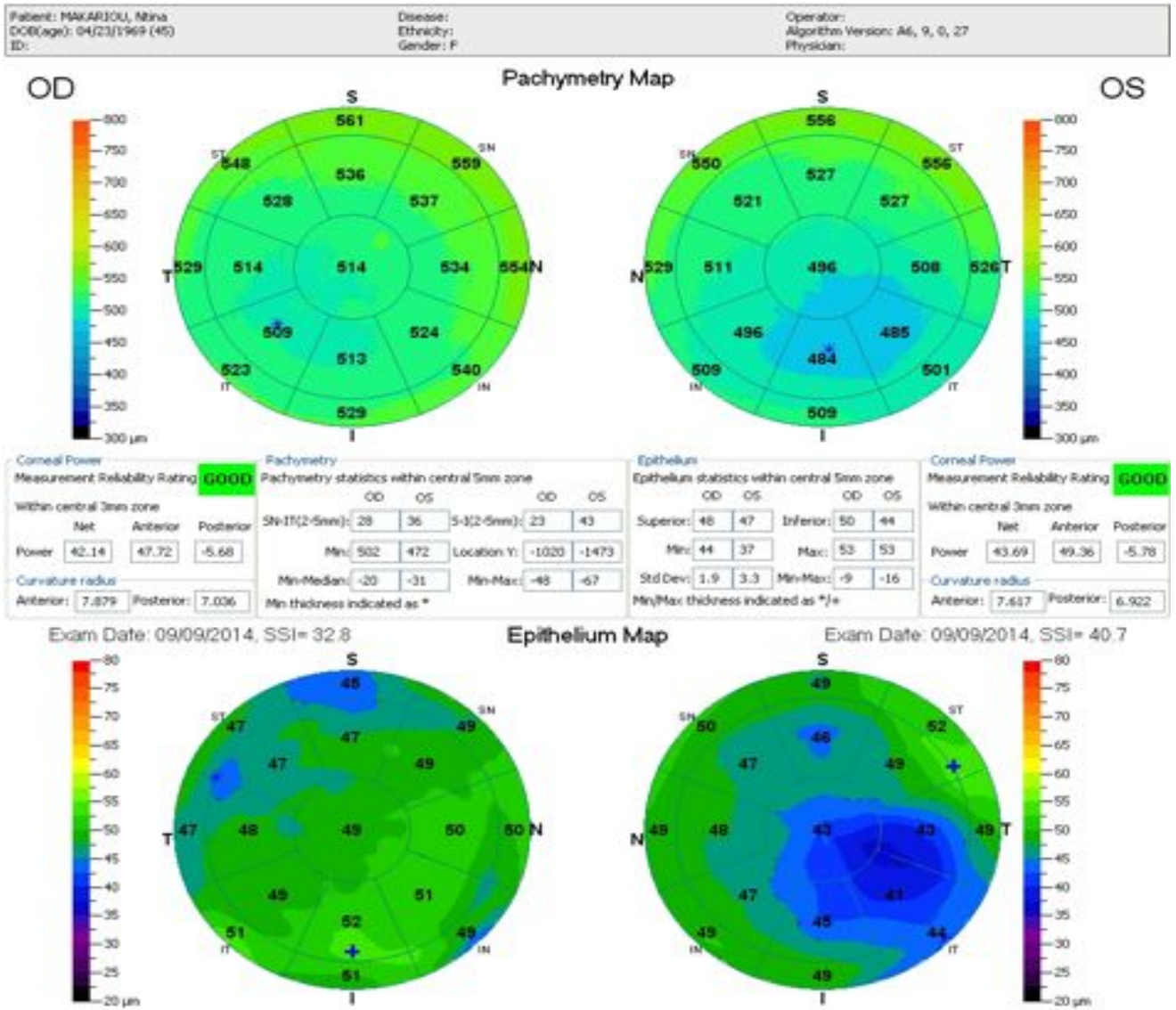

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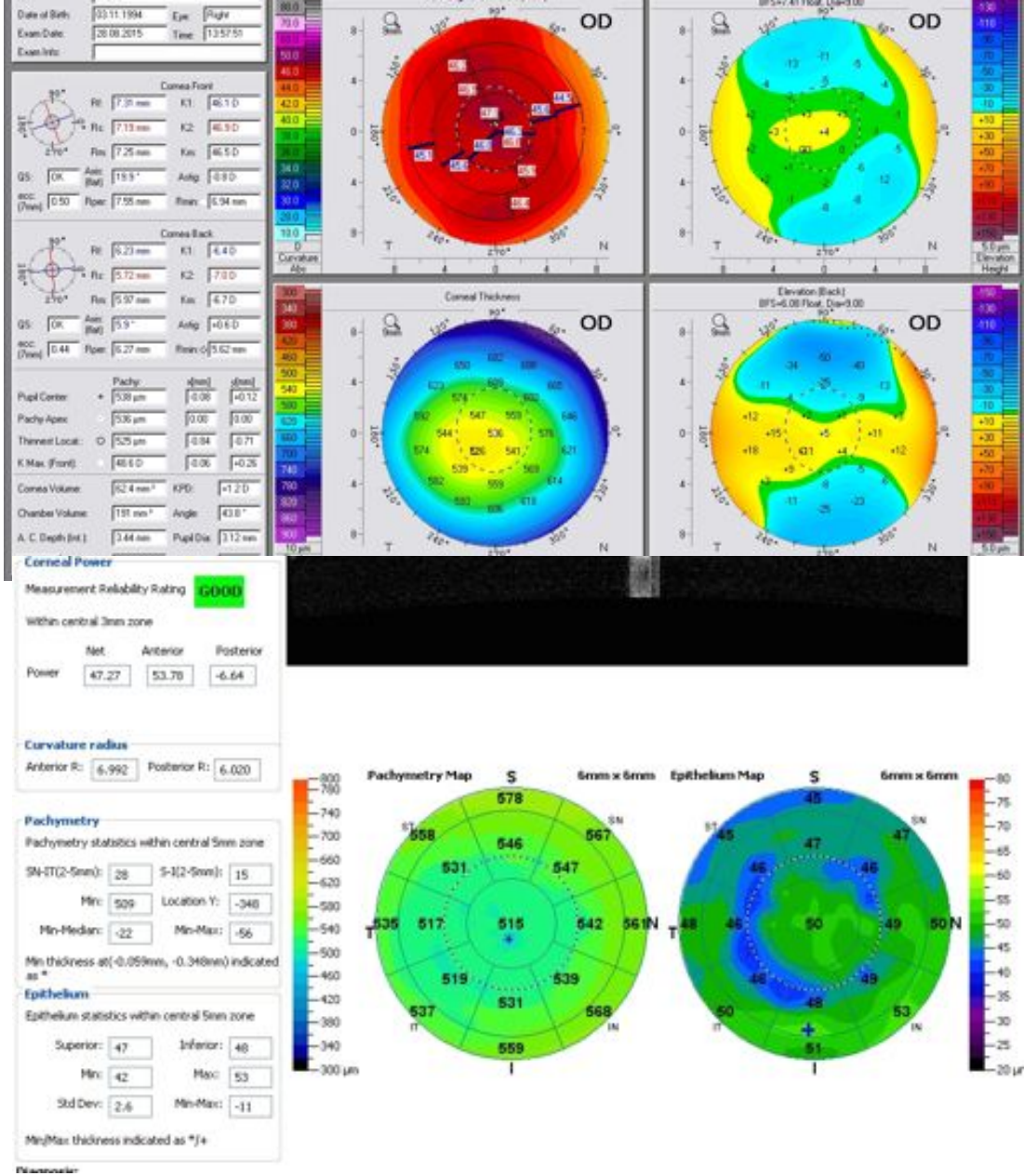

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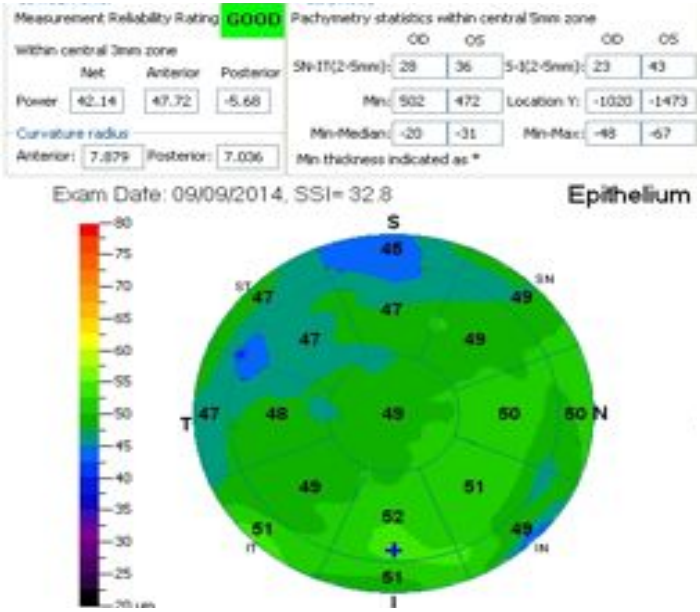

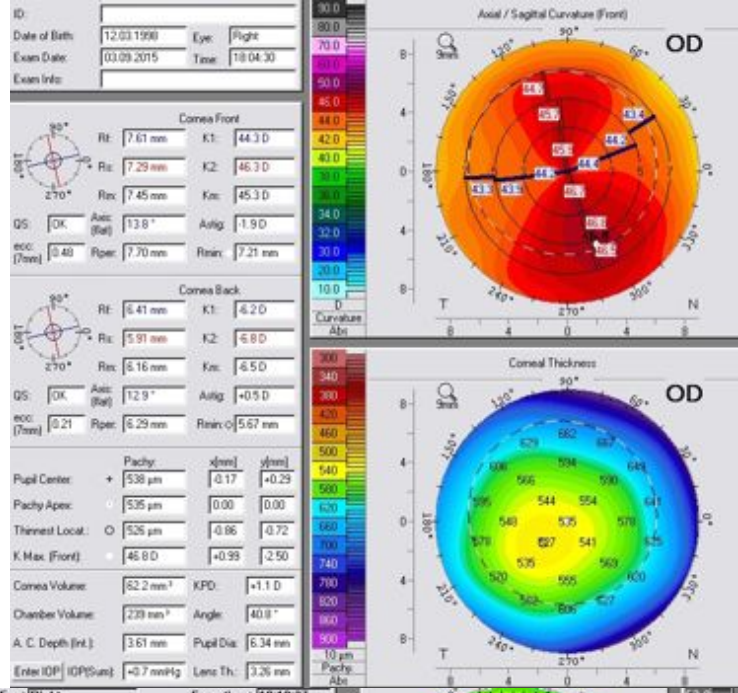

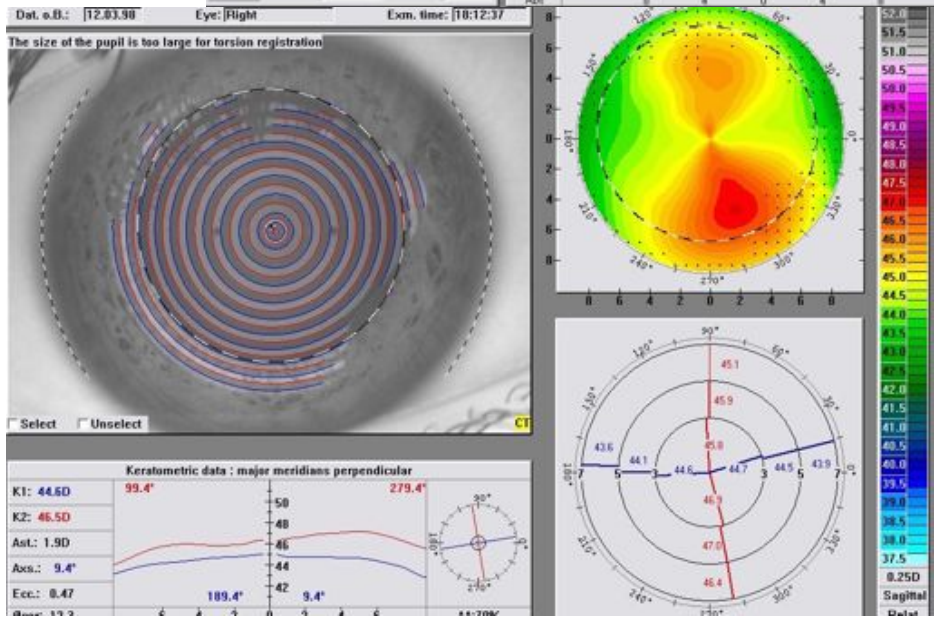

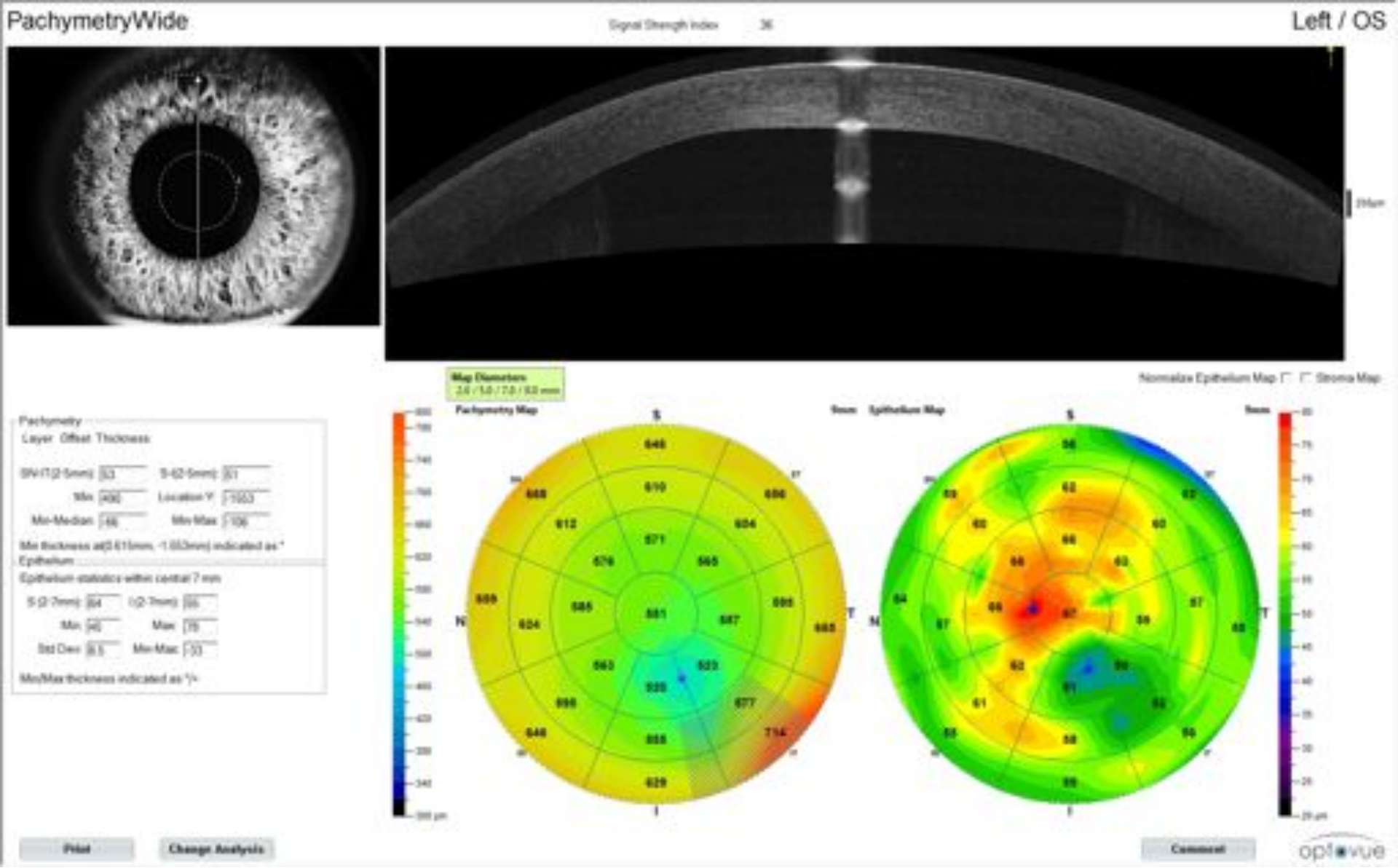

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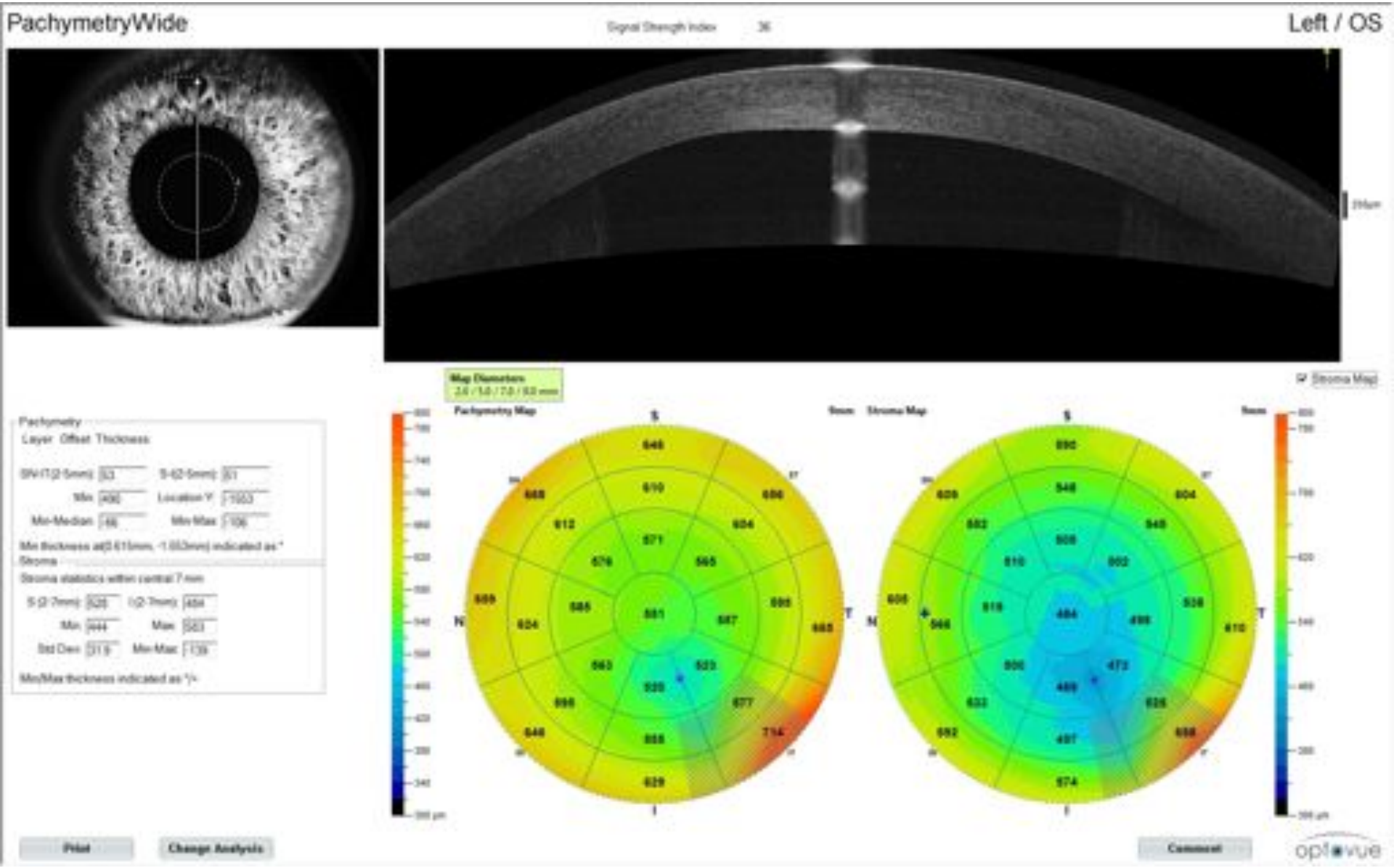

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“Currently sensitive criteria”

- Topometric asymmetry indices IHD and ISV
- Pachymetric distribution asymmetry; Scheimpflug < OCT
- Epithelial profiles